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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/515,983	09/30/2005	Elan David Massey	RD 440	6315

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EXAMINER	
MA, JAMESON Q	

ART UNIT	PAPER NUMBER
1775	

NOTIFICATION DATE	DELIVERY MODE
12/08/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOmail@MiddReut.com

Office Action Summary	Application No.	Applicant(s)	
	10/515,983	MASSEY ET AL.	
	Examiner	Art Unit	
	JAMESON Q. MA	1775	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5-16,18-21,25-27,29-36 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,5-16,18-21,25-27,29-36 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/10/2010 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3, 5-16, 18-21, 25-27, 29-36 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of the fluid directing structure ‘midway between each of said cell culture chambers' as in independent claims 43 (and subsequent dependent claims) renders the claim indefinite because it is unclear as to what the orientation of the plurality of cell culture chambers is with said device. There is no such orientation or positioning of the cell culture chambers claimed as to allow one of ordinary skill in the art to ascertain what is being described by the claim.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 3, 5-16, 18-21, 29, 35, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762) in view of Lahm et al. (US 5,795,775).

Regarding limitations recited in claim 43 which are directed to the flow of a 'common well' of nutrient medium, it is noted that neither the manner of operating a disclosed device nor material or article worked upon further limit an apparatus claim. Said limitations do not differentiate apparatus claims from prior art. See MPEP § 2114 and 2115. Further, it has been held that process limitations do not have patentable weight in an apparatus claim. See Ex parte Thibault, 164 USPQ 666, 667 (Bd. App. 1969) that states "Expressions relating the apparatus to contents thereof and to an intended operation are of no significance in determining patentability of the apparatus claim."

Regarding claims 3, 5, 6 and 43, Stoppini discloses an exposure device comprising a base portion (1) connected with a top portion (3) to form therebetween a medium chamber adjacent said base portion, a fluid exposure chamber adjacent said top portion which is contiguous and coextensive with said medium chamber, and a plurality of cell culture chambers (6) positioned between said medium chamber and said culture chamber (see fig. 1: the medium chamber is viewed to be the space below membrane 5, and the fluid exposure chamber is the space above membrane 5 and are

viewed to be contiguous and coextensive with each other), said medium chamber being common to all culture chambers. The device further comprises a fluid inlet and outlet (sealing devices 4 and 4' are viewed as fully capable of acting as an inlet or outlet, as fluid flow could be initiated via a syringe or similar device) and a medium inlet and outlet (sterile septa 9' and 9" are viewed as medium inlets/outlets).

However, the reference does not explicitly disclose the device wherein the medium directing structure consisting of an island projecting from said base portion and centrally located within said nutrient medium chamber, midway between each of said cell culture chambers.

Lahm teaches a vessel and an assembly for growing cells or tissue culture in vitro, and more particularly to a vessel and an assembly wherein cells or other biological materials can be suspended within a nutrient medium (see C1/L5-9). Similar to Stoppini, Lahm teaches a cell culture chamber insert with a permeable membrane (40). Lahm further teaches that the base comprises raised protrusions (34), see fig. 2. As evidenced by figure 2, Lahm teaches a central most protrusion 34.

As it is well known in the art that culture chamber base portions can have a variety of shapes of configurations, including flat or with protrusions, (as evidenced by Stoppini and Lahm respectively), the change in configuration of shape of a device is obvious absent persuasive evidence that the particular configuration is significant. In re Dailey, 357 F.2d 669, 149 USPQ 47 (CCPA 1966). It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the culture chamber of Stoppini to include a protrusions in the base portion, as taught by Lahm. An ordinary

skilled artisan at the time of the invention would have been motivated to do the foregoing in order to increase the efficiency of heat exchange as well as simplify the manufacturing process.

It is noted that the claim recites that a fluid directing structure consists of an island projecting from said base portion. This does not exclude a device wherein there are other similarly shaped fluid directing structures, but merely that one of said fluid directing structures consists of said island, which is satisfied by Lahm.

For claim 7, the device comprises three culture chambers.

For claim 8, the base of said culture chambers are spaced apart from the base of said device by a gap, which would allow nutrient medium to flow freely under the chambers.

For claim 11, the medium inlet is located in said base portion of said device.

For claim 12, the medium inlet is located in a sidewall of said base portion.

For claims 14-16 and 18, the medium inlet is viewed as a tube, the medium outlet is spaced apart from the inlet by all of said culture chambers and the medium outlet is viewed as fully capable of removing nutrient medium from a top surface.

For claim 21, the medium outlet is viewed as a tube.

For claim 29, the fluid exposure chamber is in flow communication with all said culture chambers.

For claim 35, the device further comprises a cell culture chamber support (membrane surface 8 is viewed as a support).

Regarding claims 9-10, modified Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the length of the gap between the culture chambers and base portion. As the amount of nutrient medium and thus total nutrients available to the culture chambers are variables that can be modified, among others, by adjusting said gap length, amount of nutrient medium and thus total nutrients available to the culture chambers as the gap length is increased, the precise gap length would have been considered a result effective variable by one having ordinary skill in the art at the time the invention was made. As such, without showing unexpected results, the claimed gap length cannot be considered critical. Accordingly, one of ordinary skill in the art at the time the invention was made would have optimized, by routine experimentation, the thickness of the gap length in the apparatus of modified Stoppini to obtain the nutrient medium (and thus total nutrient capacity) of the device (In re Boesch, 617 F.2d. 272, 205 USPQ 215 (CCPA 1980)), since it has been held that where the general conditions of the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (In re Aller, 105 USPQ 223).

Regarding claim 13, modified Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the medium inlet located in a bottom wall of the base portion. The reference only discloses the inlet in a side wall of the base portion. However, the placement of the medium inlet is strictly an engineering design choice that would have been obvious to one of ordinary skill in the art barring any unexpected results based on the exact placement of the inlet.

Specifically, a change in the placement of the inlets would create two identically functioning and thus equivalent embodiments. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to place the medium inlet in the bottom wall of the base portion of the device.

Regarding claims 19-20, modified Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the medium outlet comprises two outlets. However, it would have been obvious to one of ordinary skill in the art at the time of invention to add an additional medium outlet in a separate location of the device in order to allow for quicker and more efficient medium removal. Additionally, regardless of the placement of the second (or more) outlet(s), they would necessarily be positioned to allow for both basal and submersion feeding of cell cultures within the cell culture chambers.

6. Claims 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762) in view of Lahm et al. (US 5,795,775) as applied to claims 3, 5, 7-16, 18-21, 29, 35, and 43 above, and further in view of Aufderheide et al. (A method for in vitro analysis of the biological activity of complex mixtures such as sidestream cigarette smoke) and Rose et al. (US 4,792,378).

Regarding claims 30-34, modified Stoppini discloses all of the claim limitations as set forth above. The reference does not explicitly disclose an additional fluid dispersing means. Aufderheide discloses that studies of the cytotoxicity of air contaminants such as gaseous particles have traditionally used animal experiments because of the

difficulties in exposing cell cultures directly to these substances (see abstract). Aufderheide further discloses that the Cultex system allows for the direct exposure of cigarette smoke to human bronchial epithelial cells to allow dose-dependent effects to be measured (see abstract).

Rose discloses a gas dispersion disk (20) that includes an arrangement of apertures which are tailored to the particular pressure gradients existing within a reactor chamber to thereby provide a uniform flow of gas vapors to the various objects below it (see C4/L52-63).

It would have been obvious to one of ordinary skill in the art at the time of invention to provide a gas (fluid) dispersing means in a portion of the device of modified Stoppini, in order to provide a means for in vitro toxicology testing. This would allow for the dose-dependent measurement of cigarette smoke effects to human bronchial cell in vitro, as taught by Aufderheide. It would have further been obvious to one of ordinary skill in the art at the time of invention to use the fluid dispersion disk of Rose in the apparatus of modified Stoppini, in order to create a uniform distribution of gas (fluid) flow over the cell cultures. The use of a dispersion disk would necessitate that it be located above the cells to allow for uniform flow distribution.

Aufderheide further teaches that the fluid inlet is connected to a fluid generating means (see figure 7: smoking machine).

7. Claims 25-27 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762) in view of Lahm et al. (US 5,795,775) as applied to

claims 3, 5, 7-12, 14-16, 18-21, 29, 35, and 43 above, and further in view of Gruenberg (US 5,627,070).

Regarding claims 25-27, modified Stoppini discloses all of the claim limitations as set forth above. Additionally, the reference discloses that perfusion of the nutritive medium takes place by means of an external peristaltic pump (see C2/L40-44). However, the reference does not explicitly disclose that there are two separate pumps attached to the medium inlet and outlet respectively.

Similar to Stoppini, figure 1 of Gruenberg teaches a cell growing device for in vitro cell population growth (see abstract). The device contains a recirculation mechanism (6), which contain stainless steel connectors (6a) which connect the inflow and outflow openings of cartridges (4, which are where the cells are maintained), see C10/L24-43). A centrifugal pump (44a) carries media through the stainless steel pathway to a regeneration mechanism (46) wherein media is replenished with nutrients and essential gases, and wherein waste products from cell growth are removed. A second pump (44b) directs the regenerated media to the cartridge inflow openings.

It would have been obvious to one of ordinary skill in the art at the time of invention to substitute the peristaltic pump of Stoppini, with the dual-pump recirculation/media regeneration system in order to allow the circulating media to be replenished, as taught by Gruenberg.

The two centrifugal pumps would be fully capable of operating at separate pump rates. Regarding the limitations of claim 27 which are directed to a manner of operating disclosed pump, it is noted that neither the manner of operating a disclosed device nor

material or article worked upon further limit an apparatus claim. Said limitations do not differentiate apparatus claims from prior art. See MPEP § 2114 and 2115. Further, it has been held that process limitations do not have patentable weight in an apparatus claim. See Ex parte Thibault, 164 USPQ 666, 667 (Bd. App. 1969) that states "Expressions relating the apparatus to contents thereof and to an intended operation are of no significance in determining patentability of the apparatus claim."

Regarding claim 36, Gruenberg teaches that the recirculation tubing is made from stainless steel, as disclosed above. Therefore, part of the exposure device is made from stainless steel.

Response to Arguments

8. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMESON Q. MA whose telephone number is (571)270-7063. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571)272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JM
December 2, 2010

/Michael A Marcheschi/
Supervisory Patent Examiner, Art Unit 1775